

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

**Applicants:** Maria Cristina Rosa Geroni, et al.      **Examiner:** Unassigned  
**Serial No:** 10/549,714      **Art Unit:** Unassigned  
**Filed:** September 16, 2005      **Docket:** 17803 (PC27338A)  
**For:** COMBINED THERAPY COMPRISING NEMORUBICIN AND A CYCLOOXYGENASE-2-INHIBITOR      **Dated:** October 26, 2005

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

**INFORMATION DISCLOSURE STATEMENT**

In accordance with 37 C.F.R. §§ 1.97 and 1.98, it is requested that the following references, which are also listed on the attached Form PTO-1449, be made of record in the above-identified case.

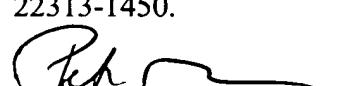
1. United States Patent No. 4,672,057, dated June 9, 1987 to Bargiotti et al.;
2. United States Patent No. 4,710,564, dated December 1, 1987 to Otake et al.;
3. European Patent Publication No. 0 434 960 A1, published July 3, 1991;

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**CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)**

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner of Patents, P. O. Box 1450, Alexandria, VA 22313-1450.

Dated: October 26, 2005



Peter I. Bernstein

4. UK Patent Publication No. GB 2 247 885 A, published March 18, 1992;
5. Lewis A.D. et al., "Role of Cytochrome P-450 from the Human CYP3A Gene Family in the Potentiation of Morpholino Doxorubicin by Human Liver Microsomes", *Cancer Research* 52(16):4379-4384 (1992), XP-001182477;
6. United States Patent No. 5,466,823, dated November 14, 1995 to Talley et al.;
7. German Patent Publication No. DE 195 47 958 A1, published June 27, 1996;
8. UK Patent Publication No. GB 2 294 495 A, published May 1, 1996;
9. United States Patent No. 5,633,272, dated May 27, 1997 to Talley et al.;
10. United States Patent No. 5,840,924, dated November 24, 1998 to Desmond et al.;
11. UK Patent Publication No. GB 2 325 067 A, published November 11, 1998;
12. PCT International Publication No. WO 98/03484, published January 29, 1998;
13. United States Patent No. 5,932,598, dated August 3, 1999 to Talley et al.;
14. Achiwa H. et al., "Prognostic Significance of Elevated Cyclooxygenase 2 Expression in Primary, Resected Lung Adenocarcinomas", *Clinical Cancer Research* 5:1001-1005 (1999);
15. Masunaga R. et al., "Cyclooxygenase-2 Expression Correlates with Tumor Neovascularization and Prognosis in Human Colorectal Carcinoma Patients", *Clinical Cancer Research* 6:4064-4068 (2000);
16. United States Patent No. 6,034,256, dated March 7, 2000 to Carter et al.;
17. PCT International Publication No. WO 00/25779, published May 11, 2000;
18. PCT International Publication No. WO 00/66093, published November 9, 2000;
19. PCT International Publication No. WO 00/38730, published July 6, 2000;
20. Rahman Md. A. et al., "Coexpression of Inducible Nitric Oxide Synthase and COX-2 in Hepatocellular Carcinoma and Surrounding Liver: Possible Involvement of COX-2 in the Angiogenesis of Hepatitis C Virus-Positive Cases", *Clinical Cancer Research* 7:1325-1332 (2001);

21. Beulz-Riche D. et al., "Metabolism of Methoxymorpholino-Doxorubicin in Rat, Dog and Monkey Liver Microsomes: Comparison with Human Microsomes", *Fundamental & Clinical Pharmacology* 15:373-378 (2001);
22. Fraier D. et al., "LC-MS-MS Determination of Nemorubicin (Methoxymorpholinyldoxorubicin, PNU-152243A) and its 13-OH Metabolite (PNU-155051A) in Human Plasma", *Journal of Pharmaceutical and Biomedical Analysis* 30(3):377-389 (2002); and
23. Quintieri L. et al., "Cellular Pharmacology of PNU-159682, a Liver Microsomal Metabolite of Methoxymorpholinyl Doxorubicin (Nemorubicin; MMDX)", *European Journal of Cancer* 38:S19 (2002), XP-004403484.

Reference nos. 3, 5, 7, 18, 19 and 23 were cited in a Search Report dated July 28, 2004 received from the European Patent Office. Applicants are submitting copies of the above-cited references, together with a copy of the Search Report. The relevance of above-identified reference nos. 3, 5, 7, 18, 19 and 23 has been described in the Search Report. The relevance of above-identified reference nos. 1, 2, 4, 6, 8-17 and 20-22 has been described in the specification.

Inasmuch as this Information Disclosure Statement is being submitted in accordance with the schedule set out in 37 C.F.R. §1.97(b), no statement or fee is required.

Respectfully submitted,



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Registration No.: 43,497

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PIB:dg

Form PTO-1449 (REV. 7-80) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		Atty. Docket No. (Optional)		Application Number			
<b>LIST OF PRIOR ART CITED BY APPLICANT</b>		17803 (PC27338A)		10/549,714			
(Use several sheets if necessary)		Applicant(s) Maria Cristina Rosa Geroni, et al.					
		Filing Date September 16, 2005		Group Art Unit Unassigned			
<b>U.S. PATENT DOCUMENTS</b>							
EXAMINER INITIAL*		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE (if appropriate)
	AA	4,672,057	6/9/87	Bargiotti et al.			
	AB	4,710,564	12/1/87	Otake et al.			
	AC	5,466,823	11/14/95	Talley et al.			
	AD	5,633,272	5/27/97	Talley et al.			
	AE	5,840,924	11/24/98	Desmond et al.			
	AF	5,932,598	8/3/99	Talley et al.			
	AG	6,034,256	3/7/00	Carter et al.			
<b>FOREIGN PATENT DOCUMENTS</b>							
REF	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
						YES	NO
	0 434 960 A1	7/3/91	EPO				
	GB 2 247 885 A	3/18/92	United Kingdom				
	DE 195 47 958 A1	6/27/96	Germany				
	GB 2 294 495 A	5/1/96	United Kingdom				
	GB 2 325 067 A	11/11/98	United Kingdom				
	WO 98/03484	1/29/98	PCT				
	WO 00/25779	5/11/00	PCT				
	WO 00/66093	11/9/00	PCT				
	WO 00/38730	7/6/00	PCT				
<b>OTHER DOCUMENTS</b> (Including Author, Title, Date, Pertinent Pages, Etc.)							
		Lewis A.D. et al., "Role of Cytochrome P-450 from the Human CYP3A Gene Family in the Potentiation of Morpholino Doxorubicin by Human Liver Microsomes", <i>Cancer Research</i> 52(16):4379-4384 (1992), XP-001182477					
EXAMINER		DATE CONSIDERED					
* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.							

**LIST OF PRIOR ART  
CITED BY APPLICANT**

(Use several sheets if necessary)

Atty. Docket No. (Optional)

17803 (PC27338A)

Application Number

10/549,714

**Applicant(s)**

Maria Cristina Rosa Geroni, et al.

**Filing Date**

September 16, 2005

**Group Art Unit**

Unassigned

**FOREIGN PATENT DOCUMENTS**

	REF	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO

**OTHER DOCUMENTS** (Including Author, Title, Date, Pertinent Pages, Etc.)

		Achiwa H. et al., "Prognostic Significance of Elevated Cyclooxygenase 2 Expression in Primary, Resected Lung Adenocarcinomas", <i>Clinical Cancer Research</i> 5:1001-1005 (1999)
		Masunaga R. et al., "Cyclooxygenase-2 Expression Correlates with Tumor Neovascularization and Prognosis in Human Colorectal Carcinoma Patients", <i>Clinical Cancer Research</i> 6:4064-4068 (2000)
		Rahman Md. A. et al., "Coexpression of Inducible Nitric Oxide Synthase and COX-2 in Hepatocellular Carcinoma and Surrounding Liver: Possible Involvement of COX-2 in the Angiogenesis of Hepatitis C Virus-Positive Cases", <i>Clinical Cancer Research</i> 7:1325-1332 (2001)
		Beulz-Riche D. et al., "Metabolism of Methoxymorpholino-Doxorubicin in Rat, Dog and Monkey Liver Microsomes: Comparison with Human Microsomes", <i>Fundamental &amp; Clinical Pharmacology</i> 15:373-378 (2001)
		Fraier D. et al., "LC-MS-MS Determination of Nemorubicin (Methoxymorpholinyldoxorubicin, PNU-152243A) and its 13-OH Metabolite (PNU-155051A) in Human Plasma", <i>Journal of Pharmaceutical and Biomedical Analysis</i> 30(3):377-389 (2002)
		Quintieri L. et al., "Cellular Pharmacology of PNU-159682, a Liver Microsomal Metabolite of Methoxymorpholinyl Doxorubicin (Nemorubicin; MMDX)", <i>European Journal of Cancer</i> 38:S19 (2002), XP-004403484

EXAMINER

DATE CONSIDERED

\* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

**TRANSMITTAL OF INFORMATION DISCLOSURE STATEMENT  
(Under 37 CFR 1.97(b) or 1.97(c))**

Docket No.  
**17803 (PC27338A)**

In Re Application Of: **Maria Cristina Rosa Geroni, et al.**

Application No.	Filing Date	Examiner	Customer No.	Group Art Unit	Confirmation No.
10/549,714	September 16, 2005	Unassigned	23389	Unassigned	Unassignd

Title:

**COMBINED THERAPY COMPRISING NEMORUBICIN AND A CYCLOOXYGENASE-2-INHIBITOR**

Address to:  
**Commissioner for Patents**  
P.O. Box 1450  
Alexandria, VA 22313-1450

**37 CFR 1.97(b)**

1.  The Information Disclosure Statement submitted herewith is being filed within three months of the filing of a national application other than a continued prosecution application under 37 CFR 1.53(d); within three months of the date of entry of the national stage as set forth in 37 CFR 1.491 in an international application; before the mailing of a first Office Action on the merits, or before the mailing of a first Office Action after the filing of a request for continued examination under 37 CFR 1.114.

**37 CFR 1.97(c)**

2.  The Information Disclosure Statement submitted herewith is being filed after the period specified in 37 CFR 1.97(b), provided that the Information Disclosure Statement is filed before the mailing date of a Final Action under 37 CFR 1.113, a Notice of Allowance under 37 CFR 1.311, or an Action that otherwise closes prosecution in the application, and is accompanied by one of:

the statement specified in 37 CFR 1.97(e);

**OR**

the fee set forth in 37 CFR 1.17(p).

**TRANSMITTAL OF INFORMATION DISCLOSURE STATEMENT  
(Under 37 CFR 1.97(b) or 1.97(c))**

Docket No.  
17803 (PC27338A)

In Re Application of: **Maria Cristina Rosa Geroni, et al.**

Application No.	Filing Date	Examiner	Customer No.	Group Art Unit	Confirmation No.
10/549,714	September 16, 2005	Unassigned	23389	Unassigned	Unassignd

Title:

**COMBINED THERAPY COMPRISING NEMORUBICIN AND A CYCLOOXYGENASE-2-INHIBITOR**

**Payment of Fee**

(Only complete if Applicant elects to pay the fee set forth in 37 CFR 1.17(p))

A check in the amount of \_\_\_\_\_ is attached.

The Director is hereby authorized to charge and credit Deposit Account No. **19-1013/SSMP** as described below.

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**October 26, 2005**

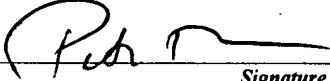
(Date)

Signature of Person Mailing Correspondence

Peter I. Bernstein

Typed or Printed Name of Person Mailing Certificate

\*This certificate may only be used if paying by deposit account.

  
Signature

**Peter I. Bernstein**  
Registration No. 43,497

Dated: **October 26, 2005**

CC: